PATENT COOPERATION TREATY

CORRECTED VERSION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

REC'D 09 NOV 2005 PCT
WIPO PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/002145	24.02.2004	

International Patent Classification (IPC) or both national classification and IPC
C12Q1/68, G01N33/574, G01N33/68, C12N15/11, A61K38/17, A61K39/00

Applicant
ONCOTHERAPY SCIENCE, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Mossier, B Telephone No. +49 89 2399-8706

Form PCT/ISA/237 (Cover Sheet) (January 2004)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-8 , 17-23 (with respect to industrial applicability) and 24, 29

because:

☒ the said international application, or the said claims Nos. 1-8 and 17- 3 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 24, 29

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15, 17-23, 26, 27, 32
	No:	Claims	16, 25, 28, 30, 31, 33-36
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15, 17-23, 26, 27, 32
Industrial applicability (IA)	Yes:	Claims	9-15, 25-28, 30-36
	No:	Claims	

2. Citations and explanations

see separate sheet

Present application discloses the use of the gene C10orf3 in the diagnosis and/or treatment of colorectal cancer (CRC). Said gene was identified by microarray expression profiling of colorectal cancers. siRNAs against C10orf3, in particular the siRNA consisting of the sequence set forth in SEQ ID NO:21, inhibit the growth of colon cancer cells. Methods of diagnosis, screening, treatment using C10orf3 as well as siRNAs are claimed.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

III.1 Claims 1 - 8 and 17 - 23 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 The following documents were taken into account:

D1: WO 01/60860 A (MILLENNIUM PREDICTIVE MEDICINE) 23 August 2001 (2001-08-23)

D2: WO 2004/001072 A (ONCOTHERAPY SCIENCE INC ; FURUKAWA YOICHI (JP); NAKAMURA YUSUKE (JP);) 31 December 2003 (2003-12-31)

D3: KITAHARA O ET AL: "ALTERATIONS OF GENE EXPRESSION DURING COLORECTAL CARCINOGENESIS REVEALED BY CDNA MICROARRAYS AFTER LASER-CAPTURE MICRODISSECTION OF TUMOR TISSURES AND NORMAL EPITHELIA" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 61, no. 9, 1 May 2001 (2001-05-01), pages 3544-3549, XP001157021 ISSN: 0008-5472

V.2 D1 discloses genes, antisense nucleic acid molecules, antibodies, compositions, kits as well as methods for the identification/therapy of human prostate cancer (page 7, line 31 - page 8, line 19; page 24, lines 6 - 26; page 35, line 14 - page 37, line 28). SEQ ID NO:21355 and SEQ ID NO:27197 show 99,9%identity with SEQ ID NO:1, respectively C10orf3 in 2616nt overlap (41-2654:10-2624). Hence, the subject-matter referred to in claims 16, 25, 28, 30 , 31 and 33 - 36 is anticipated

by D1. Said claims are therefore objected under Article 33(2) PCT.

V.3 D2, which is considered to represent the closest prior art for evaluating the inventiveness of the subject-matter referred to in claims 1 - 15 and 17 - 23, provides methods for detecting, diagnosing and treating colorectal cancers (CRC). 51 genes were identified by means of cDNA microarrays as commonly up-regulated in adenomas **and** carcinomas as compared with their normal epithelia (Abstract; Table 1) (Remark: a microarray representing 23040 genes was used).
The subject-matter referred to in claims 1 - 15 and 17 - 23 differs from D2 in that the gene C10orf3 that is up-regulated in CRC is disclosed and used as target for the treatment, diagnosis and prevention of CRC.
The problem to be solved by the present application may therefore be regarded as the provision of a further up-regulated gene in CRC that can be used as a therapeutic target.
D3 already discloses 44 genes that show up-regulated expression in colorectal cancer (CRC) compared with the corresponding noncancerous colonic epithelia and states that these genes represent a source of novel targets for cancer therapy (Abstract, Figure 2A) (Remark: a microarray representing 4420 genes was used).
It is considered to be straight forward and without the exercise of inventive skill for the person skilled in the art to either (a) screen the microarray referred to in D2 for genes that are not necessarily expressed in both, adenomas and carcinomas, but **only** in carcinomas or (b) to use the probes of D3 to screen the microarray of D2.
In both cases the provision of the gene C10orf3 represents merely the provision of a further gene that can be used for the detection, diagnosis and/or treatment of CRC whereby the selection that has effectively been made has to be considered arbitrary.
In addition, the Examining Divisions raises the Applicant's attention to the fact that in order for inventive step to be recognised for alternatives to known products and methods, it is necessary that the claimed alternatives provide a technical effect different from the prior art. Therefore, to establish an inventive activity, the provision of further gene that is up-regulated in CRC protein must be justified by the technical purpose, i.e. by a hitherto unknown or unexpected effect, caused by those technical features which distinguish the claimed molecule form numerous other ones. Thus, it is not possible to acknowledge inventive step for the application, as no technical effect of the claimed C10orf3 over prior art is revealed.
Hence, claims 1 - 15 and 17 - 23 do not appear to be inventive and are therefor objected under Article 33(3) PCT.

V.4 With regard to D1 which already refers to antisense nucleic acid molecules subject-matter referred to in claims 26, 27 and 32 is not considered to be inventive. The disclosure of said siRNA amounts nothing more than an arbitrary selection. Hence, said claims do not comply with Article 33(3) PCT (see also V.2).

V.5 For the assessment of the present claims 1 - 8 and 17 - 23 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

V.6 The term "*the biological activity of the protein encoded by C10orf3*" used in claims 3 and 12 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).